

WHAT IS CLAIMED IS:

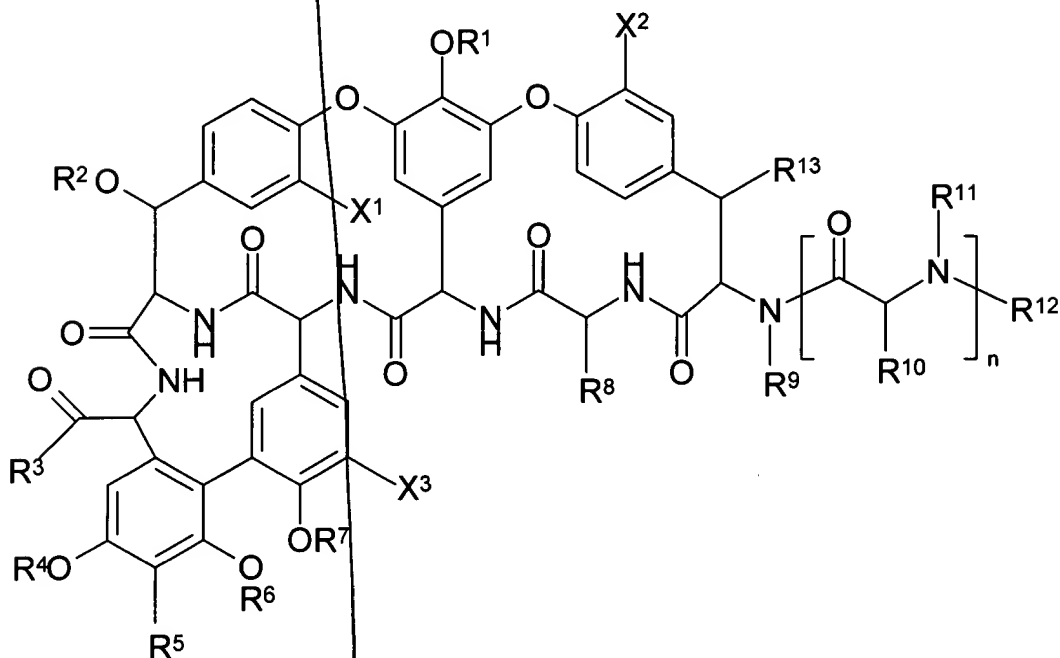
1. A glycopeptide substituted with one or more substituents each comprising one or more phosphono groups; or a pharmaceutically acceptable salt, or stereoisomer, or prodrug thereof.

5 2. The glycopeptide of claim 1, wherein the glycopeptide is substituted at the C-terminus with a substituent comprising one or two phosphono groups.

3. The glycopeptide of claim 1, wherein the glycopeptide is substituted at the R-terminus with a substituent comprising one or two phosphono groups.

10 4. The glycopeptide of claim 3, wherein the substituent at the R-terminus is N-(phosphonomethyl)aminomethyl; N-(2-hydroxy-2-phosphonoethyl)aminomethyl; N-carboxymethyl-N-(phosphonomethyl)aminomethyl; N,N-bis(phosphonomethyl)aminomethyl; or N-(3-phosphonopropyl)aminomethyl.

5. The glycopeptide of claim 1 which is a compound of formula I:



wherein:

R^1 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl, heterocyclic and $-R^a-Y-R^b-(Z)_x$; or R^1 is a saccharide group optionally substituted with $-R^a-Y-R^b-(Z)_x$, R^f , $-C(O)R^f$, or $-C(O)-R^a-Y-R^b-(Z)_x$;

R^2 is hydrogen or a saccharide group optionally substituted with $-R^a-Y-R^b-(Z)_x$, R^f , $-C(O)R^f$, or $-C(O)-R^a-Y-R^b-(Z)_x$;

R^3 is $-OR^c$, $-NR^cR^c$, $-O-R^a-Y-R^b-(Z)_x$, $-NR^c-R^a-Y-R^b-(Z)_x$, $-NR^cR^c$, or $-O-R^c$; or R^3 is a nitrogen-linked, oxygen-linked, or sulfur-linked substituent that comprises one or more phosphono groups;

R^4 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, $-R^a-Y-R^b-(Z)_x$, $-C(O)R^d$ and

a saccharide group optionally substituted with $-R^a-Y-R^b-(Z)_x$, R^f , $-C(O)R^f$, or $-C(O)-R^a-Y-R^b-(Z)_x$, or R^4 and R^5 can be joined, together with the atoms to which they are attached, form a heterocyclic ring optionally substituted with $-NR^c-R^a-Y-R^b-(Z)_x$;

5 R^5 is selected from the group consisting of hydrogen, halo, $-CH(R^c)-NR^cR^c$, $-CH(R^c)-NR^cR^c$, $-CH(R^c)-NR^c-R^a-Y-R^b-(Z)_x$, $-CH(R^c)-R^x$, $-CH(R^c)-NR^c-R^a-C(=O)-R^x$, and a substituent that comprises one or more phosphono groups;

10 R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, $-R^a-Y-R^b-(Z)_x$, $-C(O)R^d$ and a saccharide group optionally substituted with $-R^a-Y-R^b-(Z)_x$, R^f , $-C(O)R^f$, or $-C(O)-R^a-Y-R^b-(Z)_x$, or R^5 and R^6 can be joined, together with the atoms to which they are attached, form a heterocyclic ring optionally substituted with $-NR^c-R^a-Y-R^b-(Z)_x$;

15 R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, $-R^a-Y-R^b-(Z)_x$, and $-C(O)R^d$;

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 R^8 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl and heterocyclic;

20 R^9 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl and heterocyclic;

25 R^{10} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl and heterocyclic; or R^8 and R^{10} are joined to form $-Ar^1-O-Ar^2-$, where Ar^1 and Ar^2 are independently arylene or heteroarylene;

R^{11} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl and heterocyclic, or R^{10} and R^{11} are joined, together with the carbon and nitrogen atoms to which they are attached, to form a heterocyclic ring;

R^{12} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl, heterocyclic, $-C(O)R^d$, $-C(NH)R^d$, $-C(O)NR^cR^c$, $-C(O)OR^d$, $-C(NH)NR^cR^c$, $-R^a-Y-R^b-(Z)_x$, and $-C(O)-R^a-Y-R^b-(Z)_x$, or R^{11} and R^{12} are joined, together with the nitrogen atom to which they are attached, to form a heterocyclic ring;

R^{13} is selected from the group consisting of hydrogen or $-OR^{14}$;

R^{14} is selected from hydrogen, $-C(O)R^d$ and a saccharide group;

each R^a is independently selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene and substituted alkynylene;

each R^b is independently selected from the group consisting of a covalent bond, alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene and substituted alkynylene, provided R^b is not a covalent bond when Z is hydrogen;

each R^c is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl, heterocyclic and $-C(O)R^d$;

each R^d is independently selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl and heterocyclic;

R^e is a saccharide group;

each R^f is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl, or heterocyclic;

R^x is an N-linked amino saccharide or an N-linked heterocycle;

5 X^1 , X^2 and X^3 are independently selected from hydrogen or chloro;

each Y is independently selected from the group consisting of oxygen, sulfur,

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-S-S-, $-NR^c$ -, $-S(O)$ -, $-SO_2$ -, $-NR^cC(O)$ -, $-OSO_2$ -, $-OC(O)$ -, $-NR^cSO_2$ -,
-C(O) NR^c -, $-C(O)O$ -, $-SO_2NR^c$ -, $-SO_2O$ -, $-P(O)(OR^c)O$ -, $-P(O)(OR^c)NR^c$ -,
-OP(O)(OR^c)O-, $-OP(O)(OR^c)NR^c$ -, $-OC(O)O$ -, $-NR^cC(O)O$ -, $-NR^cC(O)NR^c$ -,
10 -OC(O) NR^c -, $-C(=O)$ -, and $-NR^cSO_2NR^c$ -;

each Z is independently selected from hydrogen, aryl, cycloalkyl, cycloalkenyl, heteroaryl and heterocyclic;

n is 0, 1 or 2; and

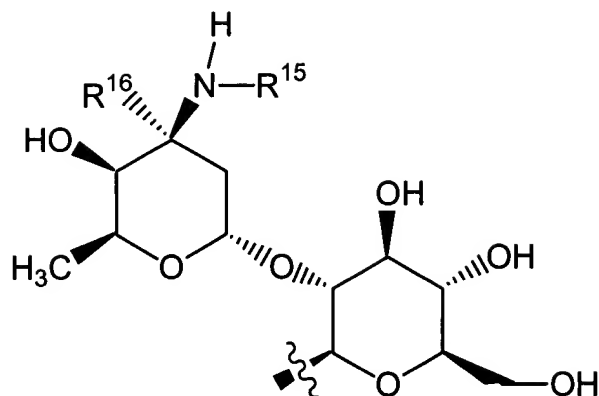
x is 1 or 2;

15 or a pharmaceutically acceptable salt, stereoisomer, or prodrug thereof;

provided at least one of R^3 and R^5 is a substituent comprising one or more phosphono groups.

6. The glycopeptide of claim 5 wherein R^1 is a saccharide group optionally substituted with $-R^a-Y-R^b-(Z)_x$, R^f , $-C(O)R^f$, or $-C(O)-R^a-Y-R^b-(Z)$.

20 7. The glycopeptide of claim 5 wherein R^1 is a saccharide group of the formula:

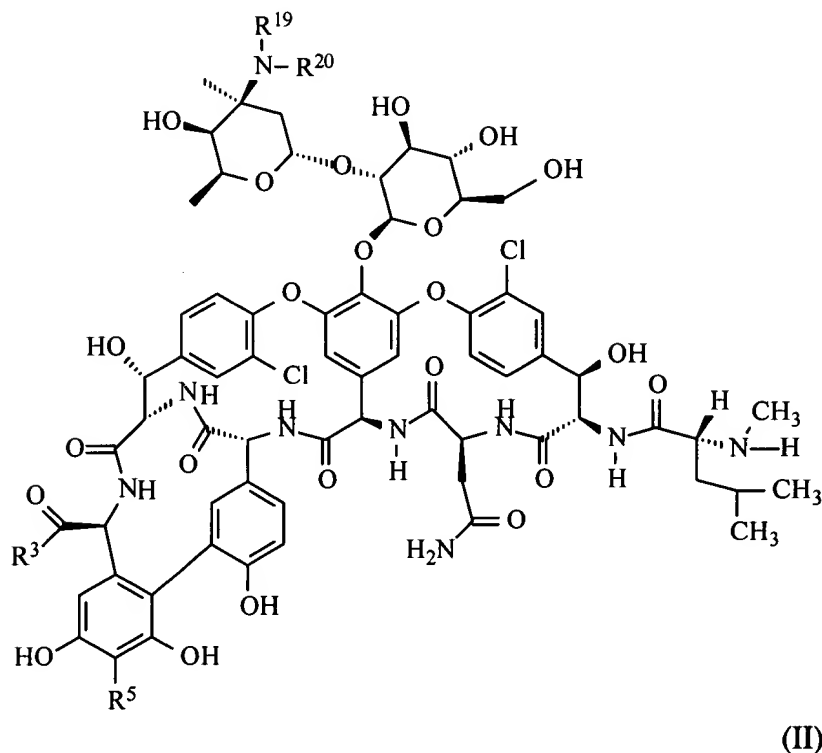


wherein R^{15} is $-R^a-Y-R^b-(Z)_x$, R^f , $-C(O)R^f$, or $-C(O)-R^a-Y-R^b-(Z)_x$; and R^{16} is hydrogen or methyl.

8. The glycopeptide of claim 6 wherein R^2 , R^4 , R^6 , and R^7 are each hydrogen.
9. The glycopeptide of claim 8 wherein R^3 is $-OH$.
- 5 10. The glycopeptide of claim 8 wherein R^3 is a nitrogen-linked, oxygen-linked, or sulfur-linked substituent that comprises one or more phosphono groups.
11. The glycopeptide of claim 10 wherein R^3 is a group of the formula $-O-R^a-P(O)(OH)_2$, $-S-R^a-P(O)(OH)_2$, or $-NR^c-R^a-P(O)(OH)_2$.
12. The glycopeptide of claim 8 wherein R^5 is a group of the formula $-CH(R^{21})-N(R^c)-R^a-P(O)(OH)_2$; wherein R^{21} is hydrogen or R^d .
- 10 13. The glycopeptide of claim 12 wherein R^5 is $-CH-NH-R^a-P(O)(OH)_2$.

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14. The glycopeptide of claim 5 which is a compound of formula II:



wherein:

R^{19} is hydrogen;

R^{20} is $-R^a-Y-R^b-(Z)_x$, R^f , $-C(O)R^f$, or $-C(O)-R^a-Y-R^b-(Z)_x$; and

- 5 R^a , Y , R^b , Z , x , R^f , R^3 , and R^5 have the values defined in claim 5;
or a pharmaceutically acceptable salt, or stereoisomer, or prodrug thereof;
provided at least one of R^3 and R^5 is a substituent comprising one or more
phosphono groups.

15. The glycopeptide of claim 14 wherein R^3 is $-OH$.

- 10 16. The glycopeptide of claim 14 wherein R^3 is a nitrogen-linked, oxygen-linked, or

sulfur-linked substituent that comprises one or more phosphono groups.

17. The glycopeptide of claim 14 wherein R^3 is a group of the formula -
 $O-R^a-P(O)(OH)_2$, $-S-R^a-P(O)(OH)_2$, or $-NR^c-R^a-P(O)(OH)_2$.

18. The glycopeptide of claim 14 wherein R^5 is a group of the formula
5 $-(CH(R^{21})-N(R^c)-R^a-P(O)(OH)_2)$; wherein R^{21} is hydrogen or R^d .

19. The glycopeptide of claim 14 wherein R^{20} is $-CH_2CH_2-NH-(CH_2)_9CH_3$;
 $-CH_2CH_2CH_2-NH-(CH_2)_8CH_3$; $-CH_2CH_2CH_2CH_2-NH-(CH_2)_7CH_3$;
 $-CH_2CH_2-NHSO_2-(CH_2)_9CH_3$; $-CH_2CH_2-NHSO_2-(CH_2)_{11}CH_3$;
 $-CH_2CH_2-S-(CH_2)_8CH_3$; $-CH_2CH_2-S-(CH_2)_9CH_3$; $-CH_2CH_2-S-(CH_2)_{10}CH_3$;
10 $-CH_2CH_2CH_2-S-(CH_2)_8CH_3$; $-CH_2CH_2CH_2-S-(CH_2)_9CH_3$; $-CH_2CH_2CH_2-S-(CH_2)_3-$
 $CH=CH-(CH_2)_4CH_3$ (*trans*); $-CH_2CH_2CH_2CH_2-S-(CH_2)_7CH_3$;
 $-CH_2CH_2-S(O)-(CH_2)_9CH_3$; $-CH_2CH_2-S-(CH_2)_6Ph$; $-CH_2CH_2-S-(CH_2)_8Ph$;
 $-CH_2CH_2CH_2-S-(CH_2)_8Ph$; $-CH_2CH_2-NH-CH_2-4-(4-Cl-Ph)-Ph$;
 $-CH_2CH_2-NH-CH_2-4-[4-(CH_3)_2CHCH_2-]Ph$; $-CH_2CH_2-NH-CH_2-4-(4-CF_3-Ph)-Ph$;
15 $-CH_2CH_2-S-CH_2-4-(4-Cl-Ph)-Ph$; $-CH_2CH_2-S(O)-CH_2-4-(4-Cl-Ph)-Ph$;
 $-CH_2CH_2CH_2-S-CH_2-4-(4-Cl-Ph)-Ph$; $-CH_2CH_2CH_2-S(O)-CH_2-4-(4-Cl-Ph)-Ph$;
 $-CH_2CH_2CH_2-S-CH_2-4-[3,4-di-Cl-PhCH_2O-]Ph$; $-CH_2CH_2-NHSO_2-CH_2-4-[4-(4-$
 $Ph)-Ph]-Ph$; $-CH_2CH_2CH_2-NHSO_2-CH_2-4-(4-Cl-Ph)-Ph$;
 $-CH_2CH_2CH_2-NHSO_2-CH_2-4-(Ph-C\equiv C-)-Ph$; $-CH_2CH_2CH_2-NHSO_2-4-(4-Cl-Ph)-Ph$;
20 or $-CH_2CH_2CH_2-NHSO_2-4-(naphth-2-yl)-Ph$.

20. The glycopeptide of claim 14 wherein R^3 is $-OH$; R^5 is $N-(phosphonomethyl)-$
aminomethyl; R^{19} is hydrogen, and R^{20} is $-CH_2CH_2-NH-(CH_2)_9CH_3$; or a
pharmaceutically acceptable salt thereof.

21. The glycopeptide of claim 14 wherein R^3 is -OH; R^5 is N-(phosphonomethyl)-aminomethyl; R^{19} is hydrogen, and R^{20} is $-\text{CH}_2\text{CH}_2\text{-NH-(CH}_2)_9\text{CH}_3$.

22. The glycopeptide of claim 20 which is the hydrochloride salt.

23. A pharmaceutical composition comprising a pharmaceutically acceptable carrier
5 and a therapeutically effective amount of a glycopeptide of any one of claims 1, 5, 14, and 20.

24. The pharmaceutical composition of Claim 23, which comprises a cyclodextrin.

25. The composition of claim 24 wherein the cyclodextrin is hydroxypropyl- β -cyclodextrin.

10 26. The composition of claim 25 which comprises from about 250 mg to about 1000 mg of the glycopeptide and from about 250 mg to about 10 g hydroxypropyl- β -cyclodextrin.

27. The composition of claim 26 wherein the weight ratio of hydroxypropyl- β -cyclodextrin to the glycopeptide is from about 1:1 to about 10:1 inclusive.

15 28. A method for preparing a glycopeptide as described claim 1 which is substituted at the C-terminus, comprising derivatizing a corresponding starting glycopeptide wherein the C-terminus is a carboxy group.

29. A method for preparing a glycopeptide as described claim 1 which is substituted at the R-terminus, comprising derivatizing a corresponding starting glycopeptide

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wherein the R_f terminus is unsubstituted.

30. A method of treating a mammal having a bacterial disease, the method comprising administering to the mammal a therapeutically effective amount of a glycopeptide of any one of claims 1, 5, 14, or 20.

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31. A method of treating a mammal having a bacterial disease, the method comprising administering to the mammal a therapeutically effective amount of a pharmaceutical composition of any one of claims 23.

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